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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/074,527	OLANDT ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,12,18 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *27* is/are allowed.

6)☒ Claim(s) *1,3-7,12,18,25,26 and 28-30* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7, 12, 18, 25-30 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 8-12-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically Examiner has withdrawn the rejections under 35 U.S.C. 112, 2nd paragraph in view of explanations provided by the applicant for "target molecule" and "a membrane". Examiner has withdrawn the rejection of claims 5-7, 25-26 under 35 U.S.C. 101, in view of the claim amendments. The rejections under 35 U.S.C. 112, 1st paragraph for lack of written description has been withdrawn in view of persuasive arguments by the applicant. Examiner has also withdrawn the objections to the specification in view of amendments provided by the applicant.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 2-7, 12, 18, 25-26 all of which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "simple sugar". The metes and bounds of this phrase is not clear to the Examiner. A perusal of the specification did not provide a specific group of sugars that the applicant considers as simple sugars. Examiner was unable to find a clear definition for said phrase in the art as well. Therefore, the above phrase renders the claim indefinite.

In response to the above rejection applicants have traversed by arguing that Examiner should refer to paragraph [0042] where the above phrase has been defined which would guide one with ordinary skill in the art to understand the types of molecules encompassed by this term. However, a perusal of the specification at the above paragraph provides definition for "ricin domain" without any remarks or definition for "simple sugar". Hence the above rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and claims 2-7, 12, 18, 25-26, 28-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide with SEQ ID NO:2 and having a specific glycosyltransferase activity (i.e., transfer sugar from UDP-glucose, UDP-N-acetylgalactosamine, GDP-mannose or CDP-abequose to substrates such as cellulose, dolichol phosphate and teichoic acid), vectors and host cells comprising said polynucleotide and a method of making said polypeptide using the host cell comprising said polynucleotide, does not reasonably provide enablement for any such polynucleotide that is at least 95% identical to SEQ ID NO:1 or 3 or any polynucleotide which encodes a polypeptide comprising an amino acid sequence of at least 90% or 95% identity to SEQ ID NO:2 having at least one activity selected from the group consisting of ability to glycosylate (i.e., transfer of any sugar from any donor) a target molecule (any type of molecule), the ability to bind to any simple sugar and the ability to attach to a membrane, vectors and host

cells comprising said polynucleotide and a method of making said polypeptide using the host cell comprising said polynucleotide, including those polypeptides comprising 285 contiguous amino acids of SEQ ID NO:2 or a polypeptide comprising a glycosyltransferase domain (amino acids 139 to 322 of SEQ ID NO:2). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1 and claims 3-7, 12, 18, 25-26, 28-30 are so broad as to encompass any polynucleotide that is at least 95% identical in its sequence to SEQ ID NO:1 or 3 and wherein said polynucleotide encodes a polypeptide not with any specific activity but with a broad activity of glycosylating (in any manner) a target molecule or simply binding to a simple sugar or have ability to bind to a membrane, followed by vectors and host cells comprising such polynucleotides and method of making the polypeptide using such polynucleotides including those polypeptides comprising 285 contiguous amino acids of SEQ ID NO:2 or a polypeptide comprising a glycosyltransferase domain (amino acids 139 to 322 of SEQ ID NO:2) . The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the

amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. Simply put, applicants have not taught those skilled in the art as to where exactly on the polynucleotide sequence of SEQ ID NO:1 or 3 specific nucleotides can be modified (i.e., by insertion, deletion or substitution), and how to select those modified sequences in order to arrive at those that encode the polypeptide having the specific activity of SEQ ID NO:2. Furthermore, it would also require undue experimentation by those skilled in the art to use polynucleotides encoding polypeptide with such highly broad activities such as glycosylate target molecule without knowing what type of sugar is transferred to what type of "target" molecule. Similarly it would be an undue burden to those skilled in the art to use the claimed polynucleotide without knowing how to use the encoded polypeptide that simply binds to "simple sugars" or "membranes". The specification is limited to teaching the use of the polynucleotide with SEQ ID NO:1 or 3 to encode the polypeptide SEQ ID NO:2 and use it as a specific glycosyltransferase capable of transferring sugar from UDP-glucose, UDP-N-acetylgalactosamine, GDP-mannose or CDP-abequose to substrates such as cellulose, dolichol phosphate and teichoic acid but provides no guidance with regard to the making of variants and mutants or with regard to the other uses indicated above. In view of the great breadth of the claim, amount of experimentation required to make and use the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a

polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known and it is routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, the positions within a polynucleotide sequence leading to variants or mutants through which amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any encoded protein, and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompasses all modifications and fragments of any polynucleotide with 95% identity to polynucleotides of SEQ ID NOS:1 and 3 or any polynucleotide which encodes a polypeptide comprising an amino acid sequence of at least 90% or 95% identity to SEQ ID NO:2 having at least one activity selected from the group consisting of ability to glycosylate (i.e., transfer of any sugar from any donor) a target molecule (any type of molecule), or the ability to bind to any simple sugar or the ability to attach to a membrane, vectors and host cells comprising said polynucleotide and a method of making said polypeptide using the host cell comprising said polynucleotide, including those polypeptides comprising 285 contiguous amino acids of SEQ ID NO:2 or a polypeptide

comprising a glycosyltransferase domain (amino acids 139 to 322 of SEQ ID NO:2), because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without affecting its activity of encoding the polypeptide having the specific glycosyltransferase activity; (B) the general tolerance of polynucleotides encoding such glycosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide on the polynucleotide with an expectation of obtaining the desired biological function; (D) specific uses for polypeptides having the activity of binding to "simple sugars" or "membranes" encoded by the claimed polynucleotides and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful .

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides with an enormous number of nucleotide modifications to SEQ ID NOS: 1 and 3 and the broad type of uses for the encoded polypeptides. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants traverse the above rejection arguing that they have amended the claim to recite 95% identity and direct the Examiner to those portions f the specification where they say they have explained to one skilled in the art as to how

to compare two sequences and what type of amino acid substitutions typically can be made without altering the activity etc. Examiner respectfully disagrees with the applicants that said argument is persuasive to overcome the above rejection. This is because, while applicants may have provided a generalized direction regarding making changes to the polypeptide or the polynucleotide, they have not taught any specific amino acid resides that can be changed. Even if they have done so, Examiner would be willing to consider only those specific sequences as enabled. However, the specification provides no such specific altered sequences of either the polynucleotide or the polypeptide. Furthermore applicants do not provide any explanation as to how those skilled in the art would use polypeptides that bind to a simple sugar or to a membrane or but simple argue that such activities are not vague. Therefore, applicants have not provided any guidance to make the variant polypeptides and polynucleotides but also not taught as to how to use polypeptides with the only activities such as binding to simple sugar and binding to a membrane. Examiner reiterates that applicants arguments are not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing and using variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance for making specific changes in the polypeptide and the polynucleotide sequences followed by the selection of which of the infinite number of variants have the claimed property (i.e., the specific glycosyltransferase activity to transfer sugar from UDP-glucose, UDP-N-acetylgalactosamine, GDP-mannose or CDP-abequose to substrates such as cellulose, dolichol phosphate and teichoic acid) and the utility of polypeptides which only bind to simple sugars and membranes (without any enzymatic function or activity). Without such guidance one of ordinary skill would be

reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the polynucleotide structure which may be modified without affecting its activity of encoding the polypeptide having the specific glycosyltransferase activity; (B) the general tolerance of polynucleotides encoding such glycosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide on the polynucleotide with an expectation of obtaining the desired biological function; (D) specific uses for polypeptides having the activity of binding to "simple sugars" or "membranes" encoded by the claimed polynucleotides and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore the above rejection is maintained.

Conclusion

Claim 27 is allowable.

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Examiner has withdrawn the previous rejections under 35 U.S.C. 102(e) in view of evidences and the Declarations filed by the applicant which are persuasive to overcome said rejection.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications. Any inquiry of a general nature or

relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

October 26, 2004